CLINICAL VIGNETTE

Cancer Risks with Multiple Sclerosis Therapies

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A 55-year-old female with a history of multiple sclerosis (MS) noted new breast changes. She had not had a screening mammogram in ten years and her last mammogram had been normal. She recently noted new left breast skin thickening and eventually an inverted nipple, which motivated her to obtain a mammogram with repeat imaging. It found skin thickening in the lower, inner quadrant of the left breast and an enlarged lymph node in the left axilla. Ultrasound done the same day noted a vague distortion of the breast parenchyma measuring approximately 8cm, with associated nipple traction and an abnormal-appearing left axillary lymph node. The findings were suspicious for primary breast malignancy with lymph node metastasis. No abnormalities were seen in the right breast. Biopsy of the distorted left breast area and the suspicious lymph node noted invasive lobular carcinoma, grade 1. The cells were estrogen receptor (ER)-positive, progesterone receptor (PR)-positive, and human epidermal receptor 2 (HER2)-positive with an immunohistochemistry of 3+ and fluorescence in situ hybridization ratio of 2.56. Given her locally advanced disease, staging computed tomography scans of the chest, abdomen, and pelvis did not show any distant metastatic disease and confirmed the known biopsy-proven abnormalities. Bone scan was also negative for metastases.

Her MS history was notable as she had been on treatment for relapsing disease with ocrelizumab for ten years. She originally started as part of a clinical trial and then as standard of care after drug approval. Since starting treatment, she had good control of her MS with no major symptoms in the last six years. Risk of breast cancer was noted as a known risk with the treatment, but there had been no instructions from her treating doctors to ensure follow up screening. The patient also had no family history of malignancy.

MS is an autoimmune demyelinating disease involving the central nervous system.[1,2] It leads to axons and myelin damage that consequently effects nerve conduction.[1] Symptoms can include paresthesias, visual changes, bowel/bladder control, or spasms.[1] The underlying cause of the disorder is unknown.[1] Treatment options have evolved over time and have included corticosteroids, interferon, mitoxantrone, azathioprine, methotrexate, cyclophosphamide, and newer immunomodulating drugs.[1,2] Currently, immunomodulating and immunosuppressive treatments are used first-line when required and continued indefinitely.[1,2] It has been proposed that the same autoimmune abnormality that leads to MS may be protective in terms of combating cancer cells, but MS treatment may undo this cancer protection.[2] Ocrelizumab, FDA approved in 2017, is a monoclonal antibody directed against CD20, a protein expressed on B cells.[2] The drug essentially depletes B cells by various mechanisms, and thus, decreases the assumed underlying autoimmune culprit.[2]

Breast cancer is the most common cancer in women.[1] The underlying cause is unknown and treatment for different subtypes of the disease has developed.[1] Prior studies have suggested a possible increased risk of breast cancer in MS patients.[1,2] However, these findings are not confirmed in all studies.[1,2] While MS's connection to cancer risks is not definitive, there is some consensus that malignancies are more common in MS patients on immunosuppressant drugs.[2] The risk is associated with family history of cancer and cumulative dose of treatment.[2] Some have even proposed that newer MS immunomodulatory drugs may have greater effects on elements of the immune system involved in cancer surveillance and thus make them larger culprits for malignancies than earlier medication classes.[1] Furthermore, newer medications are so well-tolerated they are often initiated early with patients continuing on treatment for many years.[1] Regardless, other studies have noted more aggressive breast cancer diagnoses in the MS population, which raises questions, whether there is a predisposition for higher risk breast cancer in these patients.[1]

This patient had been on immunomodulatory therapy for over a decade, but unfortunately she was also not undergoing standard screening during that time. It is impossible to know the precise factors which led to her advanced disease. Ocrelizumab was approved in 2017, but the patient started via clinical trial in 2011. Thus, her longer cumulative dose may have had an impact as well, albeit she had no family history of cancer. While it is still impossible to know the risks of cancer with immunomodulatory treatments, highlights need to emphasize the importance of age-appropriate screening for malignancies, while on these treatments given the suggested slightly increased risk.

The patient opted to proceed with neoadjuvant chemotherapy with Taxotere, Carboplatin, trastuzumab, and pertuzumab every 3 weeks for 6 cycles with plans for future mastectomy, maintenance HER2-therapy, radiation, and endocrine therapy. The patient was also advised to have future discussions with her neurologist regarding her treatment plan and how her breast cancer diagnosis may affect continuation of her ocrelizumab.

REFERENCES

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